DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Room –WO66-G609
Silver Spring, MD 20993-0002

Sientra, Inc.
% JoAnn Kuhne, MSN, RAC
VP, Regulatory Affairs and Quality Assurance
6769 Hollister Avenue, Suite 201
Santa Barbara, California 93117

MAR 19 2012

Re: P070004
Sientra Silicone Gel Breast Implants (Styles 10512-MP, 10521-HP, 20610-LP, 20621-MP/HP, 20645-LP, 20645-MP/HP, 20646-RB, 20676-E)

Dear Ms. Kuhne:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) completed its evaluation of your premarket approval application (PMA) and issued an approval order on March 9, 2012. We inadvertently made an error in omitting the following sentence regarding your post approval studies: "You also agree to participate as a stakeholder in developing the National Breast Implants Registry and contribute data from your U.S. Post-Approval Study to the Registry upon its implementation".

We hope that this omission has not inconvenienced you. If you have any questions about this corrective action, please contact David Krause, PhD at (301)-796-6970.

Sincerely yours,

Mark N. Melkerson
Director
Division of Surgical, Orthopedic
and Restorative Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

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Re: P070004
Sientra Silicone Gel Breast Implants (Styles 10512-MP, 10521-HP, 20610-LP, 20621-MP/HP, 20645-LP, 20645-MP/HP, 20646-RB, 20676-E)
Filed: September 16, 2008
Amended: May 15 and June 17, 2009; March 30, June 1, June 7, August 25, September 3, and September 30, 2010; January 24, April 25, June 13, July 14, September 15 and October 3, 2011.
Procode: FTR

Dear Ms. Kuhne:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of your premarket approval application (PMA) for the Sientra Silicone Gel Breast Implants. This device is indicated for:

- **Breast augmentation for women at least 22 years old.** Breast augmentation includes primary breast augmentation as well as revision surgery to correct or improve the result of primary breast augmentation surgery
- **Breast reconstruction.** Breast reconstruction includes primary reconstruction to replace breast tissue that has been removed due to cancer or trauma or that has failed to develop properly due to a severe breast abnormality. Breast reconstruction also includes revision surgery to correct or improve the results of a primary breast reconstruction surgery

We are pleased to inform you that the PMA is approved. You may begin commercial distribution of the device in accordance with the conditions of approval described below.

The sale and distribution of this device are restricted to prescription use in accordance with 21 CFR 801.109 and under section 515(d)(1)(B)(ii) of the Federal Food, Drug, and Cosmetic Act (the act). The device is further restricted under section 515(d)(1)(B)(ii) of the act insofar as the labeling must specify the specific training or experience practitioners need in order to use the device. FDA has determined that these restrictions on sale and distribution are necessary to provide reasonable assurance of the safety and effectiveness of the device. Your device is therefore a restricted device subject to the requirements in sections 502(q) and (r) of the act, in

addition to the many other FDA requirements governing the manufacture, distribution, and marketing of devices.

Expiration dating for this device has been established and approved at 5 years.

Continued approval of this PMA is contingent upon the submission of periodic reports, required under 21 CFR 814.84, at intervals of one year (unless otherwise specified) from the date of approval of the original PMA. Two copies of this report, identified as "Annual Report" (please use this title even if the specified interval is more frequent than one year) and bearing the applicable PMA reference number, should be submitted to the address below. The Annual Report should indicate the beginning and ending date of the period covered by the report and should include the information required by 21 CFR 814.84.

In addition to the above, and in order to provide continued reasonable assurance of the safety and effectiveness of the device, the Annual Report must include, separately for each model number (if applicable), the number of devices sold and distributed during the reporting period, including those distributed to distributors. The distribution data will serve as a denominator and provide necessary context for FDA to ascertain the frequency and prevalence of adverse events, as FDA evaluates the continued safety and effectiveness of the device.

In addition to the Annual Report requirements, you must provide the following data in post-approval study reports (PAS). Two copies, identified as "PMA Post-Approval Study Report" and bearing the applicable PMA reference number, should be submitted to the address below.

1. Post-Approval PMA Cohorts Study (PACS)
   Per agreement reached on January 11, 2012 (e-mail), this study will consist of the continued follow-up of premarket cohorts. Study participants will be followed annually for 10 years in order to assess the long-term clinical performance of your device. The Post-Approval PMA Cohorts Study (PACS) will include a total of 1,788 subjects, which includes 1,683 subjects from your Core Study and 105 subjects from the reconstruction cohorts of your Continued Access Study, who were rolled into the Core Cohort for device approval. The PACS data are to be collected via annual physician follow-up evaluations and all patients in the study will have MRI at years 6, 8, and 10. All safety and effectiveness endpoints evaluated at premarket will continue to be studied long-term. The safety endpoints include local complications, implant rupture, connective tissue diseases (CTDs), CTD signs and symptoms, lactation complications, cancer and suicide. Descriptive statistics will be provided for all endpoints. In addition, the association between the studied endpoints and your approved device will be assessed as per agreement reached on January 11, 2012 (e-mail). You are also required to conduct Device Explant Analyses for all devices retrieved from women enrolled in the PACS. You must report results of these explant analyses in the post-approval study Annual Report.

You must also update your patient and physician labeling to reflect 5 and 10-year PACS study findings on the safety and effectiveness of the device, as soon as these data are available, as well as any other time point deemed necessary by FDA if significantly new information from this study becomes available. At 6 months, 1 year, and then on an annual basis, you must submit a PACS progress report to FDA that includes: (1) the follow-up status of study subjects; and (2) a summary of findings for all study endpoints.

2. Post-approval Continued Access Study (PACAS)
Per agreement reached on January 11, 2012 (e-mail), the Post-Approval Continued Access Study (PACAS) will consist of the continued follow-up, for 5-years post-implantation, of the 2,022 subjects in the primary augmentation cohort and 475 subjects in the revision augmentation cohort enrolled in the Continued Access Study. All safety and effectiveness endpoints evaluated premarket will continue to be studied through 5-years of follow-up. Descriptive statistics will be provided. Additional analyses will be performed as per agreement reached January 11, 2012. You are also required to conduct Device Explant Analyses for all devices retrieved from women enrolled in the PACAS. You must report results of these explant analyses in the post-approval study Annual Report.

Since the last patient of the PACAS was enrolled on July 20, 2007, the follow-up of all study participants should be completed in 2012. After the completion of 5-year follow-up for all PACAS subjects, you must submit a final report to FDA that includes: patient compliance and a summary of findings for all study endpoints.

3. US Post-Approval Study (US-PAS)
Per agreement reached on January 11, 2012 (e-mail), this study is a newly enrolled cohort study in the US. The purpose of this study is to evaluate the long-term clinical performance of Sientra Silicone Gel Breast Implants under general conditions of use in the postmarket environment. Enrollment of study subjects will begin within 90 days of PMA approval. The study will enroll 4,782 women receiving Sientra Silicone Gel Breast Implants and 300 women undergoing other aesthetic surgery as the comparison group. Study subjects will be followed annually for 10 years. Data will be collected on the following safety endpoints: connective tissue diseases (CTDs), rheumatologic and neurologic signs and symptoms, cancer (lung and breast, including the potential of breast implant interference with mammography and delay of breast cancer detection), suicide/attempted suicide, local complications (including infection, rupture, and rupture rate following mammography), reoperation and implant removal, reproductive complications in women who attempt to have children, lactation complications, and congenital deformities. The effectiveness will be assessed by Gel participants' responses to questions addressing their perceived quality of life and satisfaction with their breast implants.

Data are to be collected via annual patient questionnaires. There will also be physician evaluations at years 1, 5, and 9. Descriptive statistics will be provided for the studied

endpoints. In addition, the association between the studied endpoints and your approved device will be assessed as per agreement reached on January 11, 2012. You are also required to conduct Device Explant Analyses for all devices retrieved from women enrolled in the US-PAS. You must report results of these explant analyses in the post-approval study Annual Report.

You must update your patient and physician labeling to reflect 5 and 10-year US-PAS study findings, as soon as these data are available, as well as any other time point deemed necessary by FDA if significantly new information from this study becomes available.

On a quarterly basis, you must submit a report to FDA that includes: (1) the number enrolled by subjects receiving studied device versus enrolled in comparison group; (2) the number enrolled by indication (primary augmentation, revision-augmentation, primary reconstruction, revision-reconstruction) for subjects receiving studied device; (3) the number enrolled by race/ethnicity; (4) the enrollment rates versus the stated goals; (5) the reason why eligible patients were not enrolled into the study; and (6) the follow-up rates versus the stated goals. FDA will inform you when quarterly reports are no longer necessary.

In addition, every 6 months for the first 2 years and then annually, thereafter, you are to submit a progress report that includes: (1) the status of patient enrollment as it compares to the stated goals; (2) the status of the race/ethnicity distribution as it compares to the stated goals; (3) detailed patient and device accounting; (4) the reasons why eligible patients were not enrolled into the study; (5) the follow-up rates versus the stated goals; and (6) a summary of findings for all study endpoints.

4. Post-Approval Case-Control Studies (PACCS)

Per case-control studies protocol included in P070004/A020 (submitted on October 4, 2011), the purpose of the Post-approval Case-control Studies (PACCS) is to evaluate the association between Sientra Silicone Gel Breast Implants and five rare disease outcomes (rare connective tissue diseases, neurological diseases, brain cancer, cervical/vulvar cancer and lymphoma). These studies will be conducted in Brazil and will enroll a total of 6,400 cases and 3,800 controls. For each of the five rare disease outcomes, 1,280 cases will be enrolled and compared to the controls on the history of the implantation of Sientra Silicone Gel Breast Implants.

On a quarterly basis, you must submit a report to FDA that includes: (1) the number enrolled by cases and controls; (2) the enrollment rate versus the stated goal. FDA will inform you when quarterly reports are no longer necessary. In addition, within 3 months of the completion of subject enrollment and data collection, you must submit a final PACCS study report that includes the results and conclusions of the PACCS.

5. Focus Group Study
   The purpose of the Focus Group Study is to evaluate the augmentation and reconstruction patient labeling. This will involve an independent group obtaining responses from patients on the format and content of the approved labeling. Upon completion of the focus group study, you must submit a Final Report of the focus group study findings and suggested revision of patient and physician labeling based on those findings.

In addition to the studies listed above, you must conduct non-PAS Device Explant Analyses for all Sientra Silicone Gel Breast Implants that are retrieved in the commercial setting outside the post-approval studies. On an annual basis, you must report the results of these Device Explant Analyses in the PMA Annual Reports.

Within 30 days of your receipt of this letter, you must submit PMA supplements that include the complete protocol for your post-approval studies for conditions of approval no. 1, 2, 3 and 5. Your PMA supplements should be clearly labeled as "Post-Approval Study Protocol" and submitted in triplicate to the address below. Please reference the PMA number above to facilitate processing. If there are multiple protocols being finalized after PMA approval, please submit each protocol as a separate PMA supplement.

FDA would like to remind you that you are required to submit separate PAS Progress Reports for the Post-approval studies listed above. The reports should clearly be identified as Post-Approval Study Report. Two copies for each study, identified as "PMA Post-Approval Study Report" and bearing the applicable PMA reference number, should be submitted to the address below. For more information on post-approval studies, see the FDA guidance document entitled, "Procedures for Handling Post-Approval Studies Imposed by PMA Order" (www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm070974.htm#2).

Be advised that the failure to conduct any such study in compliance with the good clinical laboratory practices in 21 CFR part 58 (if a non-clinical study subject to part 58) or the institutional review board regulations in 21 CFR part 56 and the informed consent regulations in 21 CFR part 50 (if a clinical study involving human subjects) may be grounds for FDA withdrawal of approval of the PMA.

Before making any change affecting the safety or effectiveness of the device, you must submit a PMA supplement or an alternate submission (30-day notice) in accordance with 21 CFR 814.39. All PMA supplements and alternate submissions (30-day notice) must comply with the applicable requirements in 21 CFR 814.39. For more information, please refer to the FDA guidance document entitled, "Modifications to Devices Subject to Premarket Approval (PMA) - The PMA Supplement Decision-Making Process" (www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm089274.htm).

You are reminded that many FDA requirements govern the manufacture, distribution, and marketing of devices. For example, in accordance with the Medical Device Reporting (MDR) regulation, 21 CFR 803.50 and 21 CFR 803.52, you are required to report adverse events for this device. Manufacturers of medical devices, including in vitro diagnostic devices, are required to report to FDA no later than 30 calendar days after the day they receive or otherwise becomes aware of information, from any source, that reasonably suggests that one of their marketed devices:

1. May have caused or contributed to a death or serious injury; or

2. Has malfunctioned and such device or similar device marketed by the manufacturer would be likely to cause or contribute to a death or serious injury if the malfunction were to recur.

Additional information on MDR, including how, when, and where to report, is available at www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm.

In accordance with the recall requirements specified in 21 CFR 806.10, you are required to submit a written report to FDA of any correction or removal of this device initiated by you to: (1) reduce a risk to health posed by the device; or (2) remedy a violation of the act caused by the device which may present a risk to health, with certain exceptions specified in 21 CFR 806.10(a)(2). Additional information on recalls is available at www.fda.gov/Safety/Recalls/IndustryGuidance/default.htm.

CDRH does not evaluate information related to contract liability warranties. We remind you; however, that device labeling must be truthful and not misleading. CDRH will notify the public of its decision to approve your PMA by making available, among other information, a summary of the safety and effectiveness data upon which the approval is based. The information can be found on the FDA CDRH Internet HomePage located at www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/DeviceApprovalsandClearances/PMAApprovals/default.htm. Written requests for this information can also be made to the Food and Drug Administration, Dockets Management Branch, (HFA-305), 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. The written request should include the PMA number or docket number. Within 30 days from the date that this information is placed on the Internet, any interested person may seek review of this decision by submitting a petition for review under section 515(g) of the act and requesting either a hearing or review by an independent advisory committee. FDA may, for good cause, extend this 30-day filing period.

Failure to comply with any post-approval requirement constitutes a ground for withdrawal of approval of a PMA. The introduction or delivery for introduction into interstate commerce of a device that is not in compliance with its conditions of approval is a violation of law.

You are reminded that, as soon as possible and before commercial distribution of your device, you must submit an amendment to this PMA submission with copies of all approved labeling in final printed form. Final printed labeling that is identical to the labeling approved in draft form will not routinely be reviewed by FDA staff when accompanied by a cover letter stating that the final printed labeling is identical to the labeling approved in draft form. If the final printed labeling is not identical, any changes from the final draft labeling should be highlighted and explained in the amendment.

All required documents should be submitted in triplicate, unless otherwise specified, to the address below and should reference the above PMA number to facilitate processing. One of those three copies may be an electronic copy (eCopy), in an electronic format that FDA can process, review and archive (general information: http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/PremarketSubmissions/ucm134508.htm; clinical and statistical data: http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/PremarketSubmissions/ucm136377.htm)

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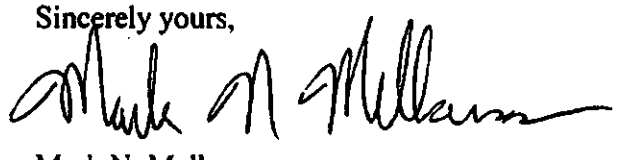
If you have any questions concerning this approval order, please contact David Krause, PhD at 301-796-6970.

Sincerely yours,



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